

REMARKS

Claims 26-28 and 30 are pending in the application. Claims 26-28 are rejected. The Applicants appreciate the Examiner withdrawing the rejection over WO 92/02256 in view of Farrar *et al.* (JNCI, 1988), Portenoy *et al.* (Pain, 1999), Stanley *et al.* (Anesth. Analg., 1989) by themselves. The Applicants responses to the remaining rejections are provided below.

CLAIM REJECTIONS BASED ON 35 U.S.C. § 103(A)

Claims 26-28 were rejected under 35 U.S.C. § 103(a), based on the Examiner's contention that they are unpatentable over WO 00/47203. The Examiner restates that WO 00/47203 "teaches formulations containing narcotic analgesics such as fentanyl citrate in combination with hydroxypropyl-beta cyclodextrin for oral administration." Furthermore, the Examiner contends that "it would have been obvious to one of ordinary skill in the art to use any fentanyl based compound with hydroxypropyl-beta cyclodextrin, with a reasonable expectation of success since it is a[n] absorption enhancer." The Applicants respectfully traverse.

The Applicants respectfully contend that WO 00/47203 does not form the basis of a proper 35 U.S.C. § 103(a) rejection because one of ordinary skill in the art would have no reasonable expectation of success in enhancing the efficacy of fentanyl by adding a cyclodextrin based on WO 00/47203. The Applicants maintain that WO 00/47203 establishing that cyclodextrins can act as oral enhancers for certain compounds would not lead one skilled in the art to assume cyclodextrins could act as oral enhancers for fentanyl-like compounds. The Applicants assert that to make a proper 103(a) rejection there must be some similarity between the structures of compounds which are orally-enhanced by inclusion in cyclodextrins and the

inventive compounds. Without such a teaching, the Applicants maintain that it is non-obvious that cyclodextrins would be suitable oral enhancers for fentanyl-like compounds. Inclusion is not *ipso facto* oral enhancement.

In addition, the Applicants also respectfully ask the Examiner not to dismiss without additional explanation the Applicants' contention that claims 26-28 are not obvious because the invention satisfies a long-felt need for oral formulations of fentanyl. Again, as described in the Applicants' communication dated June 18, 2004, fentanyl formulations have been known since the 1960s, and yet ACTIQ® is the only known FDA-approved oral formulation of fentanyl. However, ACTIQ®, a transmucosal formulation of fentanyl citrate, is not satisfactory because it causes nausea, vomiting, and/or a burning sensation in the mouth. The Applicants again strongly assert that the present invention fulfills the long-felt need for a fentanyl formulation that can be administered orally. As the Examiner is aware, a long-felt need is one of the secondary considerations that must be considered in an assessment of nonobviousness. *See* MPEP § 2141.

Accordingly, the Applicants respectfully request the withdrawal of the rejections of claims 26-28 under 35 U.S.C. 103(a) based on WO 00/47203.

Claims 26-28 were rejected under 35 U.S.C. § 103(a), based on the Examiner's contention that they are unpatentable over Farrar et al., or Portenoy et al., or Stanley et al. in combination with Chiesi et al., Bodor et al., Dwivedi et al., and WO 92/02256. The Examiner contends that the Farrar, Portenoy, Stanley and WO references each teach the efficacy of fentanyl when administered orally, and that what is lacking in these references is the teaching of the carrier cyclodextrin. Further, the Examiner contends that Chiesi et al., Bodor et al., and Dwivedi et al. show that inclusion complexes of cyclodextrins increase the solubility and bioavailability of

drugs, and that one skilled in the art would be motivated to use cyclodextrin inclusion complexes orally since WO 92 teaches preparation of inclusion complexes of fentanyl. The Applicants respectfully traverse.

While maintaining all of the arguments presented in the response to the previous action, the Applicants respectfully contend that what is missing from the cited art is the teaching that upon binding a fentanyl-like compound with a cyclodextrin an oral enhancement effect will be achieved. Even if the Examiner relies on WO 92/02256 for the encapsulation of fentanyl in cyclodextrin, this is not enough to say that this encapsulation would lead to oral enhancement. Again, inclusion is not *ipso facto* oral enhancement.

As asserted in response to the first rejection, Applicants here too contend that claims 26-28 are not obvious because the invention satisfies a long-felt need. The Applicants respectfully remind the Examiner that a long-felt need is one of the secondary considerations that must be considered in a determination of obviousness. The Applicants respectfully request the Examiner make clear he has not considered this argument.

Accordingly, the Applicants respectfully request the withdrawal of the rejections of claims 26-28 under 35 U.S.C. 103(a) based on Farrar et al., or Portenoy et al., or Stanley et al. in combination with Chiesi et al., Bodor et al., Dwivedi et al. and WO 92/02256.

DOUBLE PATENTING

Claims 26-28 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 19-26 of U.S. Patent No. 6,635,661 ("the '661 patent"). However, the compounds of '661 do not fall within the scope of the pending

claims since "y", in the pending claims, is limited to 0. In order for the compounds of '661 to be encompassed by the general formula of claim 26, "y" would have to be 1. Accordingly, the Applicants respectfully request the withdrawal of the double patenting rejections of claims 26-28 based on claims 19-26 of U.S. Patent No. 6,635,661.

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The Applicants believe they have provided for all required fees in connection with the filing of this paper. Nevertheless, the Director is hereby authorized to charge any additional required fee to our Deposit Account, 06-1448, Reference, SPV-045.01.

CONCLUSION

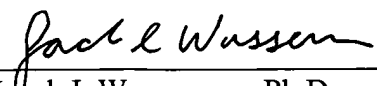
In view of the above remarks, it is believed that the pending claims are in condition for allowance. The Applicants respectfully request reconsideration and withdrawal of the pending rejections. The Applicants thank the Examiner for careful consideration of the present case. If a telephone conversation with the Applicants' Agent would expedite prosecution of the above-identified application, the Examiner is urged to contact the undersigned.

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Respectfully submitted,

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